Supplemental Methods.

Caspase-3/7 activity assay. To determine the induction of apoptosis in C57BL/6 WT and PAFR(-/-) mice following DMBA treatment, the dorsal skin of these mice were shaved and then treated with 100 µg of DMBA. After 24 hours of DMBA treatment, mice were sacrificed and a segment of mouse skin was stored in liquid nitrogen. Whole dorsal skin was scraped using a curette and homogenized in hypotonic extraction buffer containing 25mM HEPES, 5mM $MgCl_2$, 1mM EGTA, 1mM pefabloc, 1µg/ml protease inhibitors leupeptin, aprotinin and pepstatin. The samples were centrifuged and supernatants were collected. After measuring protein content, 0.5mg of total protein in 100µl was added to each well of a 96 well ELISA plate followed by adding 100µl of caspase-3/7 glo reagent (Promega, Madison WI) and incubated for 1 hour in dark prior to measurement using a SpectraMax L Luminescence microplate reader (Molecular Devices, Sunnyvale CA).

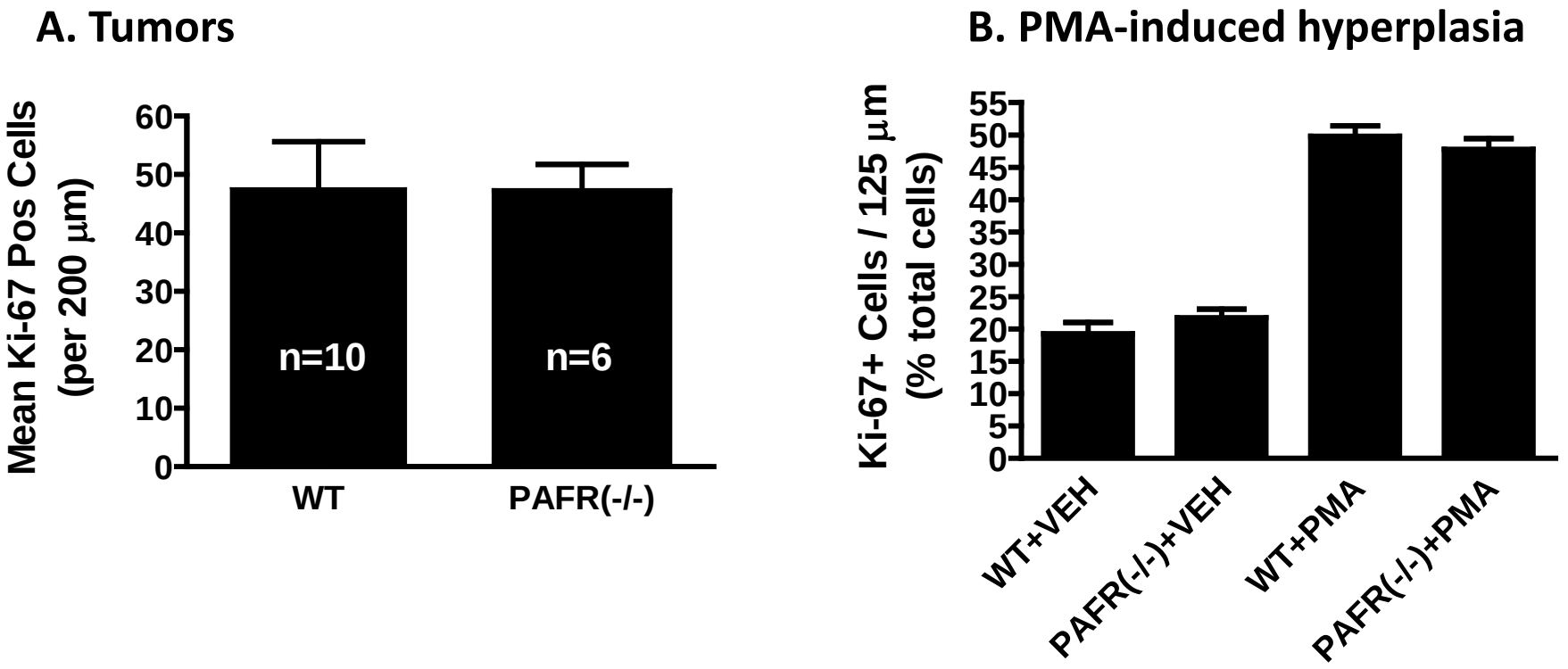
Immunohistochemistry staining for Ki-67 and H&E. For immunohistochemistry, formalin-fixed paraffin-embedded sections of mouse epidermis were deparaffinized and rehydrated. Antigen retreival was performed using 10mM citrate buffer, pH 6.0. Immunolabeling was done using monoclonal rabbit anti-Ki-67 (Clone SP6, Thermo Fisher Scientific, Fremont, CA) followed by detection using the EnVision(+) DAB visualization kit (Dako Cytomation, Inc. Fort Collins, CO). The slides were then counter-stained with hematoxylin. Ten random fields were counted in all slides, at either 200 or 400x total magnification, in a blinded manner for each condition using a Nikon Eclipse E400 microscope (Nikon Corp. Melville, NY).

SUPPLEMENTAL FIGURE LEGENDS

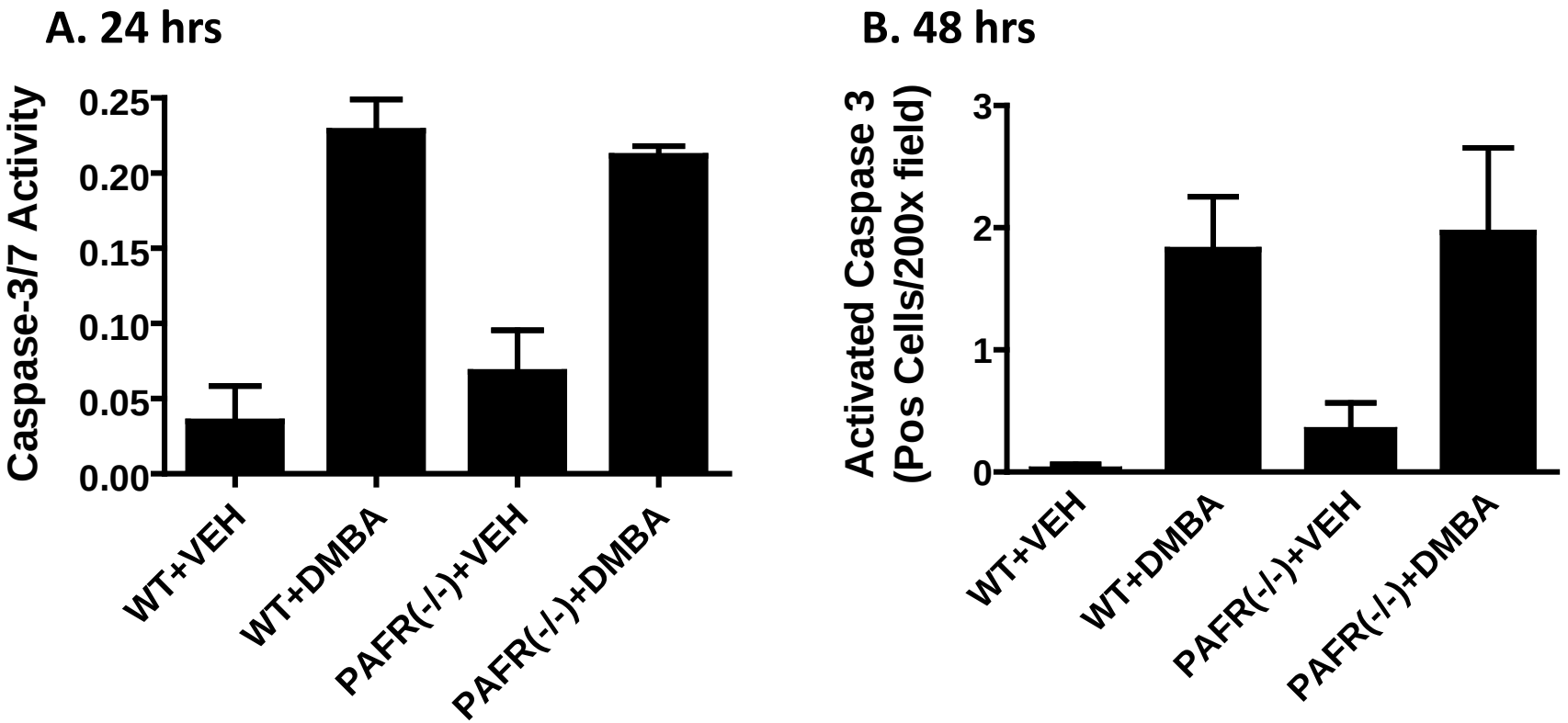
Supplemental Figure 1: **Loss of the PAFR has no effect on papilloma proliferation or on chronic PMA induced hyperplasia. (A)** Similarly sized papillomas were selected from WT and PAFR (-/-) mice treated with DMBA followed by 25 weeks of PMA treatment as described in figure 6. Five random fields were selected to count total and Ki-67 positive cells over a 200 µm linear section of the tumor as measured along the basement membrane. Data is represented as the mean Ki-67 positive cells ± SD from 6-10 different mice per group. **(B)** The dorsal epidermis of WT or PAFR (-/-) mice were treated with vehicle or 40 nmole of PMA twice weekly on non-consecutive days for 17 days. On day 18, the mice

were sacrificed and treated dorsal epidermis excised and fixed in 10% buffered formalin. Following immunolabeling, Ki-67 positive cells and total hematoxylin labeled cells were counted from five randomly selected fields for each vehicle and PMA treated WT and PAFR(-/-) mouse (6-10 mice per group) and presented as a percentage of total cells per 125 μm of epidermis (measured along the basement membrane).

Supplemental Figure 2: **DMBA-treated PAFR(-/-) exhibit no difference in apoptosis from their control littermates.** The dorsal back skin of WT or PAFR(-/-) mice were shaved and 100 μg of DMBA was applied in 0.2 ml acetone topically. **(A)** After 24 hours, mice were sacrificed and treated dorsal epidermis was excised and analyze for caspase 3/7 activity from protein lysates (0.5mg) extracted from the scrapped epidermis using a fluorogenic assay kit. Data are the mean ± SD of 4 WT and PPARγ(epi(-/-)) mice. **(B)** Similarly, WT and PAFR(-/-) mice were treated with 100 μg of DMBA and after 48 hours, mice were sacrificed and treated dorsal epidermis was bisected at the midline overlying the spinal column and fixed in 10% buffered formalin and caspase-3 stained slides were produced to quantitate caspase-3 positive cells in the epidermis from five randomly selected areas under 200x field. Data are the mean ± SD of 3-6 WT and PPARγ(epi(-/-)) mice.



Supplemental figure 1



Supplemental figure 2A&B